

PHARMACOLOGY IN MEDICINE

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THE IMPACT OF PHARMACOLOGY ON MEDICINE

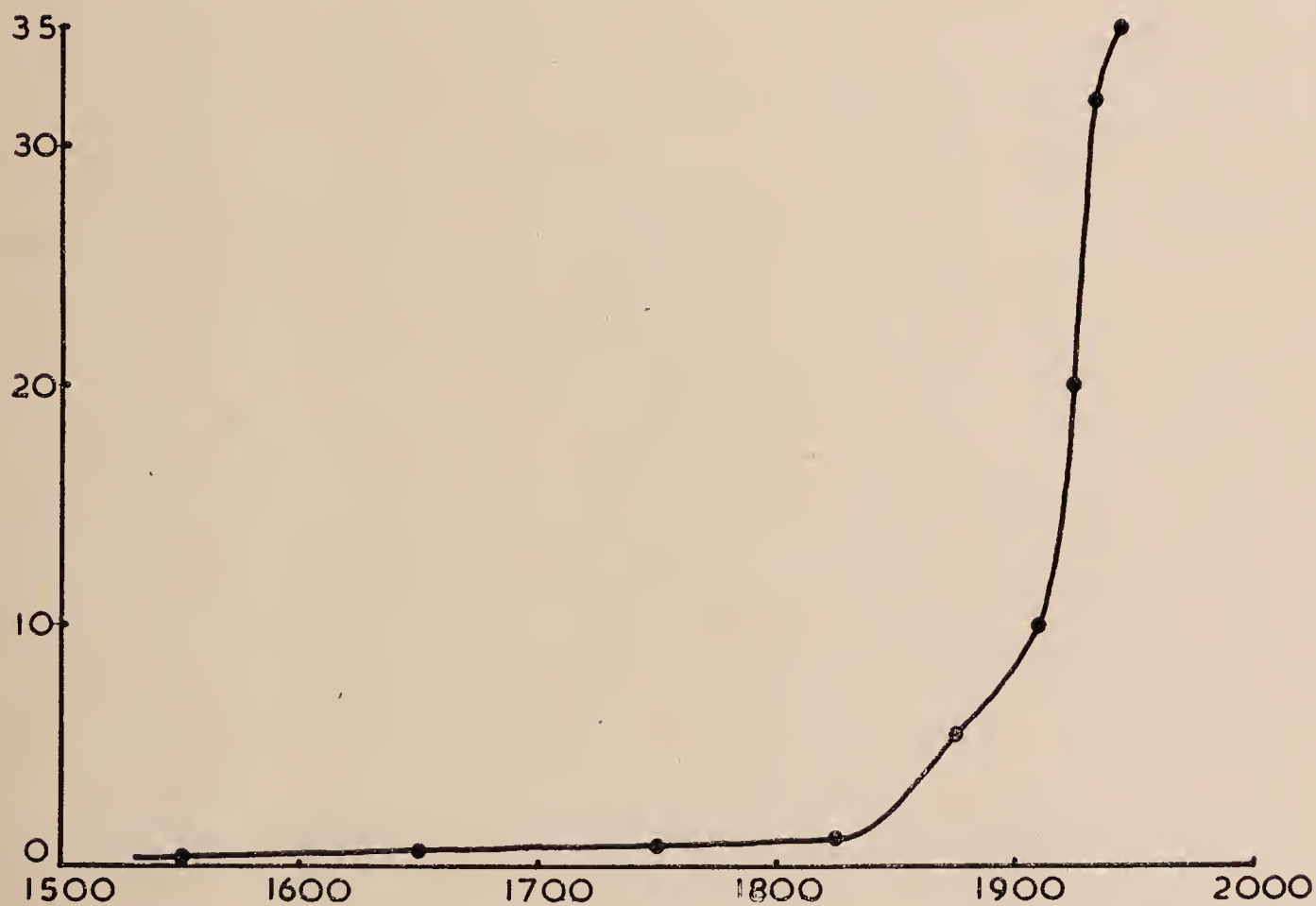
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In the last fifty years pharmacology and chemotherapy have produced a transformation in medical practice as great as that achieved by the discovery of anaesthesia or of the bacterial origin of disease. Before 1900 the specific remedies at the general practitioner's disposal did not greatly exceed the handful of classical drugs handed down to us

fully into practice. But since that period there has been a steady and accelerating accumulation of therapeutic agents, so that now one must assume that each year there will be discovered several new drugs, with new properties, allowing a new approach to a particular disease or diseases. It is difficult to assess in any quantitative way

NEW MAJOR REMEDIES PER 10 YEARS



Graph of the increasing rate of discovery of new major remedies, with lapse of time (based on Table I).

from distant generations, such as purgatives, opium, foxglove, ipecacuanha, belladonna, mercury and iodides. There were some preliminary inklings of the treatment of nutritional defect, foreshadowed by observations such as those of the naval surgeon James Lind on the value of lemons in scurvy. These observations, however, were not so well founded as to be incorporated

remedy in clinical practice to be discovered with greater precision and speed than in the past. A further major element has been the growth of the pharmaceutical industry, who have shouldered the great task of developing screening programmes from which emerge those drugs best suited for clinical practice. Between the "academic" departments and those in industry can be seen growing

how such progress is likely to continue. But it needs only the consideration of the attached table (Table 1), and the figure based on it (Fig. 1), to make one suspect that the discovery of new specific remedies is to some extent a self-generating process. As a new line of investigation is opened up, it paves the way in turn for yet other approaches, rather than leading to exploration, completion and then abandonment of a particular avenue.

This growth has come about by the steady development of the experimental method, chiefly in the sciences of chemistry, biochemistry, physiology and pathology, all assisting and stimulating one another. An important factor, too, has been a development of statistical method and the technique of clinical trial, allowing the worth of a



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<i>Date</i>	<i>Local and General Anæsthesia</i>	<i>Central stimulants and depressants</i>	<i>Autonomic</i>	<i>Neuromuscular</i>	<i>Immunotherapy and Chemotherapy</i>
Before 1850	N ₂ O Ether Chloroform	Opium Willow Caffeine Strychnine	Ephedrine Belladonna		Vaccination Quinine Mercury Iodide Ipecacuanha Filix Mas Santonin Chaulmoogra
1850-1860		Bromides		Curare	Permanganate
1860-1870		Chloral Apomorphine		Eserine	Phenol
1870-1880					Thymol
1880-1890	Cocaine	Codeine			Rabies vaccine Disinfectants
1890-1900	Orthocaine	Aspirin	Hyoscine		Typhoid vaccine Diphtheria antitoxin Tetanus antitoxin Cholera vaccine Anthrax serum
1900-1910	Procaine Stovaine	Barbiturates Picrotoxin	Adrenaline		Arsphenamine Pertussis vaccine
1910-1920					Disinfectants (Acriflavine Eusol, Chloramine T) Dysentery serum Benzyl benzoate
1920-1930	Nupercaine	Bromethol Amytal Ethylene Leptazol Nikethamide			Scarlet fever antitoxin Tryparsamide Suramin Pamaquin Chiniofon Acetarsol
1930-1940	Divinyl ether Evipan Thiopentone Cyclopropane Amethocaine	Phenytoin Pethidine	Antiadrenalin Methacholine Carbachol Amphetamine	Neostigmine	Sulphonamide Mepacrine Diamidines Alum toxoid Typhoid serum
1940-1950	Lignocaine	Antiparkinsonians Methadone Mephensesin Tridione Primidone Nalorphine	Isoprenaline Dihydroergotamine Dibenamine Hexamethonium	Muscle relaxants (d-tubocurarine, Gallamine, Decamethonium, Succinylcholine) Tensilon	PAS Sulphonamide Penicillin Streptomycin Chloramphenicol Chlortetracycline Neomycin
1950-		Chlorpromazine Reserpine Tranquillising drugs	Ganglion-blocking agents	Pyridostigmine Cholinesterase	Isoniazid Tetracyclines Erythromycin

<i>Alimentary</i>	<i>Heart and Circulation</i>	<i>Kidney</i>	<i>Endocrine</i>	<i>Nutrition</i>	<i>Miscellaneous</i>
osom salt oes mna ubarb stor oil otion oil arcoal entian	Digitalis	Alkaline diuretics Caffeine		Cod liver-oil Lemons Liver Iron	Ergot Expectorants
					Chrysarobin
	Amyl nitrite				
	Nitroglycerine				
quid paraffin					
	Strophanthus	Hexamine	Thyroid	Vitamin B	X-rays
aolin enolphthalein ntacids	Papaverine		Pituitary		Cinchophen Radium CO ₂
				Vitamin A (carotene)	Phenylhydrazine
		Mersalyl	Insulin Parathyroid Gonadotrophin Thyroxine	Liver Nicotinic acid Vitamin E	
agnesium trisilicate	Digoxin Quinidine	Mandelic acid	Estrins Stilboestrol Progesterone Thyrotrophic hormone P.Z. Insulin	Vitamin D Riboflavin Vitamin K Vitamin P	Ergometrine Heparin
ethantheline	Plasma expanders Veratrum alkaloids Procaine amide		ACTH Adrenal hormones	Intravenous iron Vitamin B ₁₂ Folic acid	Antihistamines Disulfiram Dimercaprol Mutagens Dicoumarol Phenylbutazone
otion-sickness remedies		Diamox Mercurials	Lente Insulins Aldosterone Prednisolone Synthetic oxytocin		Pholcodine

s far as possible) when it was introduced effectively. When a number of similar remedies has appeared the prototype may be mentioned and the remainder grouped.

a profitable symbiosis whereby (for instance) a possible avenue may be revealed by one partner and its full exploitation developed by the other. All this growth has resulted in a major contribution to the rising standard of medicine.

It may be questioned, however, whether this dramatic change has been wholly for the better. It is worth considering some of the criticisms that

presence or absence of bacteraemia by blood culture after the patient had received an antibiotic). Finally, a doctor, deluged with literature about new remedies, may well question how far any of them will, in fact, survive the test of time. Anyone who delves below the surface of therapeutics soon appreciates that many drugs have a natural history, beginning with a phase of increasing



Fig. 2

The rise and fall of the use of gold in the treatment of tuberculosis recorded by the number of papers published on the subject each year. (From Hart, 1945.)

could be put forward. First, it could be remarked that the old drugs handed down from the ages are still among the most important in medicine, if not, indeed, its backbone. It is remarkable that although therapeutics has developed so greatly, yet morphine, digitalis and belladonna can still be used as they were by our forefathers. Further, it could be suggested that the multiplicity of remedies now available may actually be harmful. Some of them are potentially dangerous, and from time to time it is suggested that their net effect on the survival and health of patients is even a deleterious one. Another consequence of the multiplication of drugs is that the profusion available for treatment may distract the attention of the doctor from the first duty of accurate diagnosis. It is certainly a pity that there are such a vast number of drugs and an even greater list of names in some fields (such as the antihistamines), where there is little difference between them and their number simply serves to confuse the practitioner. Most important, too, are the new medical problems which now occur in medicine: problems such as that of organisms resistant to antibiotics becoming able to invade new territories (e.g. staphylococcal enteritis); or the late results of a disease which was previously rapidly fatal (such as the sequelæ of tuberculous meningitis); or even the difficulty of diagnosis in the presence of some new drug (e.g. the attempt to establish the

interest when first introduced, then a period of fairly accepted usage, next a period of increasing scepticism, and eventually its abandonment. The use of gold therapy in the treatment of tuberculosis (Fig. 2) provides a standing warning of such a process. It is abundantly clear that in some diseases, such as ordinary "rheumatism," peptic ulcer, or the common cold, in which the ætiology is obscure, and psychological factors have unusual play, almost any remedy can cure a very substantial proportion of patients. (But this so-called "placebo" action can be recognised and controlled. It is a problem only with diseases of this type and with the major diseases the evidence of the effectiveness of a remedy is usually unequivocal.)

Despite doubts of this sort about the recent advance of therapeutics, they probably represent little more than an understandable nostalgia for a simpler life. Nobody who can compare the course of a lobar pneumonia as it used to be before the days of antibiotics and as it is now, who has witnessed the achievements of endocrine therapy, who has experienced surgical operation by old and by modern methods, or who has seen the revolution in the treatment of tuberculosis, can really wish to put this particular clock back.

But problems there certainly are, of which two must be mentioned here. The first is that of knowing how further advance in therapeutics from the pharmacological side can be fostered in



the most profitable direction. In the development of new specific remedies a pharmacology department, whether academic or industrial, occupies a crucial position. It is true that research in many other departments, particularly those of physiology and biochemistry, are of great importance in the background of the development of a new drug. But in general the interest and the incentive to undertake the development itself are lacking in such departments. Further, even when the interest is there, the special training needed for the analysis of the actions of a drug in the body and for its preparation for use in man, are not usually to be found. But if pharmacology departments have to carry the main responsibility for the development of new remedies they must be given the support to enable them to do this. Accordingly, the growth of independent pharmacology departments alongside companion departments of the other basic medical sciences, is of the greatest importance and urgency. It may be stressed that such growth will be lacking in its full fruit if the friendly liaison with other departments does not grow too. Pharmacology, more than the other medical sciences, is responsive to contacts both at the preclinical and at the clinical levels. It requires to be able to seek help or criticism not only from biochemist, physiologist and pathologist, but also from medical and surgical units. A main task in directing the growth of therapeutics along a healthy path is to ensure that independent and well-supported pharmacology departments are established, which possess at the same time immediate and easy contacts both with their laboratory colleagues and with their colleagues in the wards.

The second problem which arises is, perhaps, a more formidable one than has yet been appreciated. If there is going to develop every year a handful of new and important drugs, how is the doctor, once his training is complete, to keep in touch with such recent advances? The medical journals, indeed, perform a function of peculiar importance in the annotations on recent researches which they prepare. These probably meet the situation of those for whom it is important to know that a particular treatment is available. But it is hardly satisfactory for those who wish to know more than this, particularly if they wish, themselves, to conduct the treatment. For the doctor, whose responsibility is to be up to date not only in general principles, but also in details of practice, the annotations in the literature fall short of what he needs; while, on the other hand, the reading of the original papers or personal experiment and clinical trial must usually be impracticable. If this is so, the conclusion seems inevitable that there ought to be available, for those who wish it, some system of postgraduate teaching, whereby both the basic science involved in a new advance as well as the details of practical use should be described by people with the appropriate experience. Postgraduate teaching, therefore, becomes steadily more important as the realm

of therapeutics expands, and as it becomes impossible to give a man during his preclinical years all the basic and practical knowledge which he will come to need in the years after qualification. At present postgraduate teaching is focused on those who, having qualified, perhaps done some resident jobs and military service, then wish to specialise, and are working for advance degrees. But the usefulness of postgraduate teaching could be greatly increased if it were made available for any medical man who wished to refresh his understanding of the more recent therapeutic advances.

The succeeding articles describe some of the methods used in pharmacological laboratories, and some of the problems concerned in teaching. From these, from the expansion of the therapeutic armoury, and from the new inklings that the central nervous system is (so to say) opening up to pharmacological attack, the conclusion seems just that, in Aldous Huxley's recent phrase, "Pharmacology is on the march."

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ROYAL MEDICAL BENEVOLENT FUND

The 120th Annual General Meeting was held at the Medical Society of London on Tuesday, June 5, 1956, at 5 p.m., the President, Lord Webb-Johnson, in the Chair. The Secretary read the notice convening the meeting. Honorary officials for the ensuing year were then elected, namely, Lord Webb-Johnson, as President, F. A. Juler, C.V.O., F.R.C.S., as Hon. Treasurer, and R. Cove-Smith, M.B., M.R.C.P., as Hon. Secretary. Sir Zachary Cope, Mr. F. A. Juler, Sir Arthur MacNalty and Mr. W. H. C. Romanis, retired members, were re-elected to the Committee of Management, and a new member, Dr. S. J. Hadfield, was also appointed. Messrs. Deloitte, Plender, Griffiths & Co. were re-elected Honorary Auditors.

The Annual Report showed that the total number of beneficiaries for the year 1955 rose to 686. The total expenditure of the main fund is now more than £44,400 per annum, and during the year 1955 expenditure exceeded income by £1,190. Further donations and subscriptions are therefore urgently needed if the standard of work already being done is to be maintained, and, as these annual reports indicate, the scope of the fund is continually increasing. If only subscribers would execute a Deed of Covenant, their subscriptions, though standing at the same level, would become twice as valuable to the Fund. Any subscribers, therefore, who have not signed a Covenant are urgently requested to do so.

CLEAN AIR ACT

The Clean Air Act, which went on to the Statute Book on July 4, is a comprehensive measure of 37 sections and four schedules. The National Smoke Abatement Society has just published a Summary of the Act, which, as a 12-page booklet, describes and explains the Act in a handy form for general reference.

The booklet is available from the Society at Palace Chambers, Bridge Street, London, S.W.1, at 6d. for single copies, or 4s. 6d. per dozen, postage included.

